A comparative study of low molecular weight heparin in management of acute pancreatitis vs conventional treatment a prospective comparative clinical study

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ABSTRACT

Background: Acute pancreatitis (AP) is a common disease with varying severity. The present study was conducted to compare low molecular weight heparin and conventional treatment in the management of acute pancreatitis.

Materials & Methods: 80 patients of acute pancreatitis of both genders were randomly divided into 2 groups of 40 each. Group I patients underwent conventional therapy and group II patients were managed with administering low molecular weight heparin (LMWH) 1 mg/kg twice daily from admission until day 7 by subcutaneous injection. Parameters such as mean duration of stay, APACHE II scores on admission and at 1 week after treatment was determined.

Results: Group I had 17 males and 23 females and group II had 18 males and 22 females. Group I had 9.2 days and group II had 12.3 day of hospital stay. The difference was significant (P< 0.05). The mean APACHE in group I and group II, at admission was 0-5 seen in 5% and 14%, 6-10 in 45% and 32%,   11-15 in 20% and 28% and 16-20 in 30% and 26%. At day 7 was 0-5 seen in 56% and 23%, 6-10 in 24% and 37%, 11-15 in 15% and 30% and 16-20 in 5% and 10% respectively. The difference was significant (P< 0.05). 95% in group I and 100% in group II recovered whereas 5% in group I died. The difference was significant (P< 0.05).

Conclusion: The APACHE II Scores were found to be less in the group treated with LMWH. It offered better cure rate and lower incidence of complications.

Key words: acute pancreatitis, APACHE, low molecular weight heparin

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Eur. Chem. Bull. 2023, 12(Special Issue 1), 2116-2120

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Introduction

Acute pancreatitis (AP) is a common disease with varying severity. Mild AP has an uneventful course with spontaneous recovery in <1 week. Moderately severe and severe AP (MSAP) is associated with local and systemic complications, notably, necrosis (sterile or infected) and organ failure (transient or persistent). Infected necrosis and persistent organ failure have poor prognosis.[1]

After premature activation of pancreatic proteases and extravasation of these activated digestive enzymes into the pancreas and peripancreatic tissues, cytokines and other inflammatory mediators are produced and released with excessive leukocyte activation.[2] They stimulate the inflammatory cascade, leading to systemic inflammatory response syndrome. Proinflammatory cytokines, such as tumor necrosis factor (TNF)-α and interleukin (IL)-1β, IL-6, and IL-8, increase the capillary permeability with fluid loss, aggravating pancreatic injury. TNF-α damages the acinar cells and is probably responsible for pancreatic necrosis (PN) and damage to other organs, such as lungs, liver, intestine, and spleen. The reported mortality rate in SAP is 7%–15%.[3]

Low molecular weight heparin (LMWH) has antithrombin activity and inhibits the inflammatory cascade by reducing the release of cytokines and inflammatory mediators.[4] Moreover, heparin administration downregulates TNF-α-induced leukocyte rolling, blocks the adhesion of leukocytes to the endothelium by inhibiting the interactions between expressed adhesion molecules and endothelial cells and reduces the activation of platelets. In addition, LMWH reduces the formation of microthrombi and improves microcirculation.[5]The present study was conducted to compare low molecular weight heparin and conventional treatmentin the management of acute pancreatitis.

Materials & Methods

The present study comprised of 80 patients of acute pancreatitis of both genders. All were enrolled after they agreed to participate in the study.

Data such as name, age, gender etc. was recorded. They were randomly divided into 2 groups of 40 each. Group I patients underwent conventional therapy such as management of shock, fluid and electrolytes management, fasting, gastrointestinal decompression, antibiotics (carbapenems and metronidazole) and symptomatic treatment. Group II patients were managed with administering Low molecular weight heparin (LMWH) 1 mg/kg twice daily from admission until day 7 by subcutaneous injection. Parameters such as mean duration of stay, APACHE II scores on admission and at 1 week after treatment was determined.Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table I Distribution of patients

Groups	Group I	Group II
Method	Conventional	LMWH
M:F	17:23	18:22

Table I shows that group I had 17 males and 23 females and group II had 18 males and 22 females.

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Table II Comparison of duration of stay

Groups	Mean (days)	P value
Group I	9.2	0.01
Group II	12.3	

Table II shows that group I had 9.2 days and group II had 12.3 day of hospital stay. The difference was significant (P< 0.05).

Table II Comparison of APACHE score

APACHE	Variables	Group I	Group II	P value
At admission	0-5	5%	14%	0.05
	6-10	45%	32%	
	11-15	20%	28%	
	16-20	30%	26%	
At day 7	0-5	56%	23%	0.04
	6-10	24%	37%	
	11-15	15%	30%	
	16-20	5%	10%	

Table III, graph I shows that mean APACHE in group I and group II, at admission was   0-5 seen in 5% and 14%, 6-10 in 45% and 32%, 11-15 in 20% and 28% and 16-20 in 30% and 26%. At day 7 was 0-5 seen in 56% and 23%, 6-10 in 24% and 37%, 11-15 in 15% and 30% and 16-20 in 5% and 10% respectively. The difference was significant (P< 0.05).
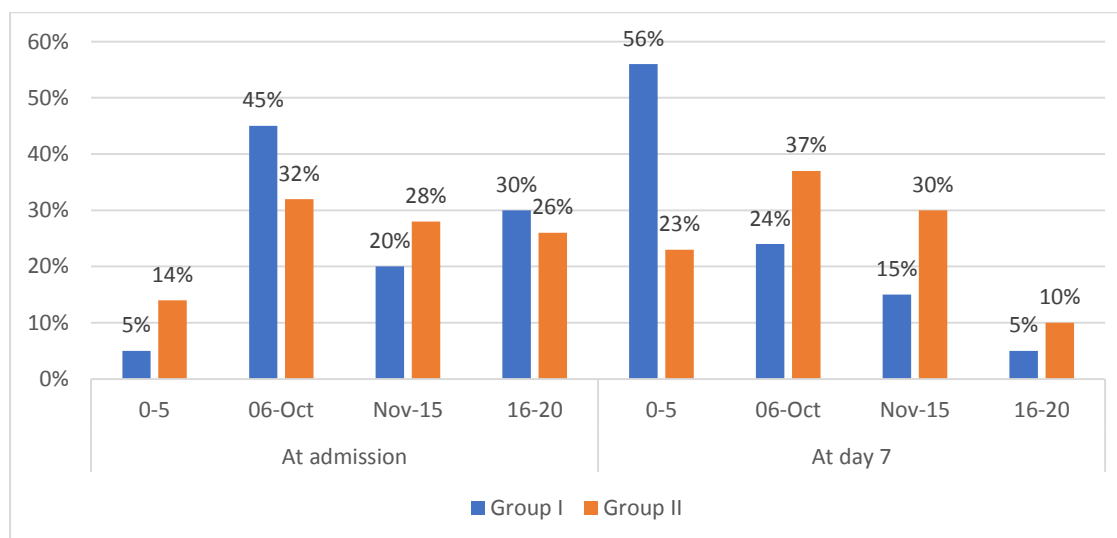
Graph IComparison of APACHE score

Table IV Assessment of outcome

Outcome	Group I	Group II	P value
Recovered	95%	100%	0.02
Died	5%	0	

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Table IV shows that 95% in group I and 100% in group II recovered whereas 5% in group I died. The difference was significant (P< 0.05).

Discussion

Acute pancreatitis runs a severe course in a minority of patients; however, this subset is responsible for the burden of the disease.[6] Therefore, decreasing the burden of AP can only be achieved with successful management strategies toward SAP.[7,8] The present study was conducted to compare low molecular weight heparin and conventional treatment in the management of acute pancreatitis.

We found that group I had 17 males and 23 females and group II had 18 males and 22 females. Group I had 9.2 days and group II had 12.3 day of hospital stay. Kumar et al[9] found that in low molecular weight heparin group, 60% had score of 0- 5, 28% had score of 6-10, 8% had score of 11-15, 4% had score of 16-20. In conventional group, 26% had score of 0-5, 34% had score of 6-10, 32% had score of 11-15, 8% had score of 16- 20. The mean duration of hospital stay in days in Low molecular weight in heparin group was 9.0 ± 2.65 and in conventional group was 12.52 ± 5.21. There was a statistically significant difference observed with relation to duration of stay between the groups. In low molecular weight heparin group mean APACHE Score at day 7 was 5.46 ± 3.91 and in conventional group was 8.58 ± 4.81.

We found that mean APACHE in group I and group II, at admission was 0-5 seen in 5% and 14%, 6-10 in 45% and 32%, 11-15 in 20% and 28% and 16-20 in 30% and 26%. At day 7 was 0-5 seen in 56% and 23%, 6-10 in 24% and 37%, 11-15 in 15% and 30% and 16-20 in 5% and 10% respectively. Tozlu et al[10] determined the effect of low molecular weight heparin (LMWH) for the prevention of pancreatic necrosis (PN) in moderately severe and severe AP (MSAP) in 100 cases. The mean age±SD of the patients (46 male and 54 female) was 52±19 years (range, 17–100). There were 50 patients in each group. On admission, clinical and laboratory parameters and Balthazar CT scores were similar between the groups. Initially, PN was present in one patient in the LMWH group and two in the SC group. Over the course, PN developed in 3 (6.1%) patients in the LMWH group and 11 (22.9%) in the SC group (p<0.05). Local and systemic complications were significantly lower in the LMWH group (p<0.05). No hemorrhagic complication occurred. Mortality was not significantly different between the groups

We found that 95% in group I and 100% in group II recovered whereas 5% in group I died. Lu et al[11] performed a randomized trial to study the effect of LMWH in the prevention of PE in 256 patients with SAP. The results indicated that LMWH markedly decreases the PE incidence and improves the survival rate in SAP. Jiao et al[12] showed that LMWH decreases the white blood cell count and increases the arterial blood partial oxygen pressure of patients with AP. In another study, they showed that LMWH decreases TNF-α and ET-1 and has a positive effect on morphological changes and vascular flow in rats with SAP.[13]

The limitation the study is small sample size.

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Conclusion

Authors found that the APACHE II Scores were found to be less in the group treated with LMWH. It offered better cure rate and lower incidence of complications.

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